REMARKS

I. Amendments to the Claims

Claims 10-28 are pending, with claims 10 and 17-23 being independent. Claims 10 and 12-28 have been amended, all without prejudice to pursue canceled subject matter, if any, in a continuing application, and without disclaimer of any subject matter.

All claims have been amended to delete references to a "particulate immunogen" or an "immunogen in particulate form." Instead, the present claims now recite that the immunogen is "in the form of aggregates, clusters, micelles, virosomes, or rosettes, or a mixture of two or more of the foregoing." Support for this amendment can be found, among other places, in the specification on page 4, lines 19-22.

The term "characteristic" has been deleted from claims 10, 14, and 17-20. In accordance with the Examiner's suggestions, the claims now recite, for example, "heat-labile enterotoxin of E. coli" (claim 10) and "[the] immunogen is from a microorganism" (claim 14). *See* Office Action dated November 7, 2003, at 3-4. Applicants agree with the Examiner that this language will not limit the source of the heat-labile enterotoxin or immunogen. *Id.* at 4 (stating that the adopted language "will include the scope of the claim that Applicant desires, i.e., recombinant as well as naturally obtained[.]").

Claim 13 has been amended to delete the word "derived," in accordance with the Examiner's suggestion. *See* Office Action at 4. Applicants agree with the Examiner that the present claim language will not limit the source of the immunogen of claim 13. As stated by the Examiner, "[a] particulate antigen from at least one infective agent

means that the agent is from the pathogenic organism regardless if it is produced from a non-pathogenic organism." *Id.*

Claims 18 and 20 have been amended to replace "induction of a common mucosal immune response" with "activating the common mucosal immune system." Support for this amendment can be found, among other places, in the specification on page 5, lines 19-23.

II. Claim Rejections Under 35 U.S.C. § 112

A. "Particulate Immunogen"

Claims 10-28 have been rejected under 35 U.S.C. § 112, ¶ 2, as allegedly being indefinite for reciting "particulate immunogen." Office Action at 2.

Without acquiescing to the allegation that the term renders the claims indefinite, Applicants have amended the pending claims to delete reference to "particulate immunogen" and "immunogen in particulate form." Accordingly, this rejection should be withdrawn as moot.

B. "Characteristic of *E. coli*" and "Characteristic of a Micro-Organism"

Claims 10, 16, and 18-20 have been rejected under 35 U.S.C. § 112, ¶ 2, as allegedly being vague and indefinite for reciting "characteristic of *E. coli.*" Office Action at 3. Claim 14 has also been rejected under the same standard for reciting "characteristic of a micro-organism." *Id.* at 4.

Without acquiescing to the allegation that "characteristic" renders the claims indefinite, Applicants have amended the claims to delete the term. Accordingly, this rejection should be withdrawn as moot.

C. "Derived"

Claim 13 has been rejected under 35 U.S.C. § 112, ¶ 2 as allegedly being indefinite for reciting "derived." Office Action at 4.

Without acquiescing to the rejection, Applicants have amended claim 13 to delete "derived." Accordingly, this rejection should be withdrawn as moot.

D. "Common Mucosal Immune Response"

Claims 18 and 20 have been rejected under 35 U.S.C. § 112, ¶ 2, as allegedly being vague and indefinite for reciting "common mucosal immune response." Office Action at 5.

Without acquiescing to the rejection, Applicants have replaced the rejected language with "activating the common mucosal immune system." This language finds literal support in the specification, together with clear disclosure of its meaning. For example, the specification states, "Remarkably, it was found that by i.n. immunisation according to the present invention the so-called common mucosal immune system is activated which results in secretion of S-IgA not only at the site [of] application (i.n.) but also in distant mucosal tissues (e.g. in the vaginal mucosal tissue)." Specification at 5, ll. 19-23 (emphasis added).

Accordingly, this rejection should be withdrawn.

III. Claim Rejections Under 35 U.S.C. § 102

Claims 10 and 12-26 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by *Tamura et al.* (U.S. Patent No. 5,182,109). Office Action at 5. Applicants respectfully disagree with this rejection.

Tamura et al. does not describe immunogens in the forms set forth in the present claims. Amended claim 10 recites, "wherein said at least one immunogen is in the form of aggregates, clusters, micelles, virosomes, or rosettes, or a mixture of two or more of the foregoing." Each independent claim contains similar language. Accordingly, to anticipate the pending claims, *Tamura et al.* must describe those forms. *See* M.P.E.P. § 2131 (stating that anticipation requires a prior art document to describe each and every claim limitation as set forth in the claim).

The Examiner points out that *Tamura et al.* teaches Japanese encephalitis vaccines that contain virus particles. However, *Tamura et al.* discloses a vaccine comprising a protein, not virus particles: "Japanese encephalitis vaccine: a vaccine comprising the whole or part of an antigenetic protein which is obtained by culturing a virus intracerebrally in mice and purifying the virus particles by centrifugation or ethyl alcohol and inactivating the same, or by genetic engineering technique or chemical synthesis." *Tamura et al.*, col. 9, ll. 17-22 (emphasis added). Thus, once virus particles are obtained, they may be subject to centrifugation, which separates solid matter from soluble matter. The use of ethyl alcohol suggests immunogens similar to those

obtained according to the method of *Davenport et al.* *See* Amendment Accompanying RCE, filed July 14, 2003, at 16. "Genetic engineering technique" does not inherently describe particulate immunogens, and "chemical synthesis" suggests single molecule synthesis. Therefore, Applicants submit that *Tamura's* disclosure does not describe immunogen "in the form of aggregates, clusters, micelles, virosomes, or rosettes, or a mixture of two or more of the foregoing."

In addition, Applicants maintain that *Tamura et al.* does not describe adjuvant free from A subunit as set forth in Applicants' claims. In fact, *Tamura et al.* describes CTB that is "≥95 %" free of A subunit. *See* Amendment Accompanying RCE at 17 (quoting SIGMA CHEMICAL COMPANY CATALOGUE 505-06, 2002-2003).[1] Dr. Tamura himself admitted that his adjuvant contained about 0.1% cholera toxin. *See id.* (citing *Tamura et al., Vaccine* 12(5):419-26, 424 (1994)).

Finally, while *Tamura et al.* compares LT and LTB in Example 14, *Tamura et al.* does not describe to the skilled artisan that the LTB must be free of A subunit. No evidence has been shown that the ordinary skilled artisan would assume the need for a purity higher than the "≥95 %" CTB likely used in *Tamura's* Example 1. That a skilled artisan could use an LTB of higher purity is merely speculative, and is not supported by

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1 The Examiner correctly points out that it is not directly known whether the CTB used by Dr. Tamura in 1989 is the exact same CTB sold by Sigma Chemical Co. in 2002-03. Office Action at 8. However, Applicants respectfully submit that the later product predicts the likely maximum purity of the earlier product. First, both products were sold by the same company. Second, both products were tested by SDS-PAGE. *See Tamura et al.* at col. 10, ll. 27-28; *see also* SIGMA CHEMICAL COMPANY CATALOGUE at 506. Third, it is counterintuitive that Sigma would have sold a purer product in 1989, and a less-pure product in 2002-03.

substantial evidence on this record. *See* M.P.E.P. § 2144.03 (requiring PTO findings of fact to be supported by substantial evidence).

For these reasons, *Tamura et al.* does not describe Applicants' claimed invention, and this rejection should be withdrawn.

IV. Claim Rejections Under 35 U.S.C. § 103

Claims 10-28 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over *Tamura et al.* in view of any one of *Hirst et al.* (WO 90/06366), *Kikuta et al.* (*Vaccine,* 8:595-599 (1990)), *Hirabayashi et al.* (*Vaccine,* 8:243-248 (1990)), or *Fujisawa et al.* (U.S. Patent No. 5,241,053). Office Action at 8. Applicants respectfully disagree with this rejection.

To establish a *prima facie* case of obviousness, the alleged prior art references when combined must teach or suggest all of the claim limitations, among other requirements. *See* M.P.E.P. § 2143.

The *prima facie* case fails here at least because the alleged prior art does not teach or suggest the forms of the immunogens now claimed. Each independent claim recites that the immunogen is "in the form of aggregates, clusters, micelles, virosomes, or rosettes, or a mixture of two or more of the foregoing." In addition, each independent claim states that "said at least one immunogen is not covalently coupled to said B subunits." Not one of the cited documents teaches or suggests these forms of immunogen.

Tamura et al., Kikuta et al., and *Hirabayashi et al.* all use soluble HA antigen isolated according to the method of *Davenport et al.,* which method produces non-particulate immunogens. *See* Amendment Accompanying RCE at 16, 18; *see also* specification at 3, ll. 23-28. *Hirst et al.* and *Fujisawa et al.* both teach fusion protein immunogens, in which the immunogen is covalently bound to the B subunits. *See* Amendment Accompanying RCE at 17, 19. Thus, none of the cited documents teach an immunogen that is not covalently bound to the B subunit, wherein the immunogen is in the form of aggregates, clusters, micelles, virosomes, or rosettes, or a mixture of two or more of the foregoing.

Because the cited documents do not, alone or in combination, teach or suggest all of the claim limitations, a *prima facie* case cannot be built on their disclosures. Therefore, this rejection should be withdrawn.

V. Possible Interview

Applicants believe that this application is close to allowance, since they have adopted many of the Examiner's suggestions. If the Examiner has questions, or perceives only minor obstacles to allowance, the Examiner is invited to contact the undersigned at (202) 408-4331 for an informal discussion or to set up an interview.

CONCLUSION

Applicants respectfully request reconsideration of this application in view of the amendments and remarks set forth above and the timely allowance of all pending claims.

Please grant any extensions of time required to enter this Amendment and charge any fees required under 37 C.F.R. §§ 1.16 or 1.17 to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
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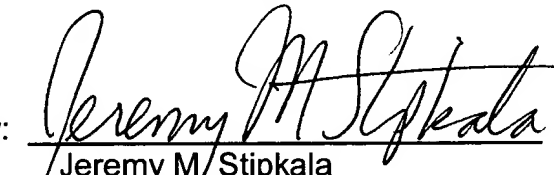
Dated: February 5, 2004

By: 
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